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Dermatoglyphic features of Familial Mediterranean Fever patients

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Abstract
Aim: Dermatoglyphic signs are associated with genetic and environmental factors. The skin patterns of the hands can give clues about the presence of various diseases. Familial Mediterranean fever (FMF) is an inherited disease characterized by periodic recurrent fever, abdominal or joint pain. In this study, we aimed to find out if there are dermatoglyphic findings specific to FMF disease.
Material and Method: This study was performed between June 2018 and January 2019 in Departments of Medical Genetics and Anatomy, Cumhuriyet University School of Medicine, Sivas, Turkey. The dermatoglyphic data of 40 FMF patients, and 40 healthy controls were obtained with a digital scanner. For these populations, atd, dat, adt angles, a-b ridge count, sample types of all fingers, and ridge counts were calculated with the ImageJ program. Results: The number of fingertip lines and a-b ridge count were higher in the patients than in the control group. The angle of palm atd was higher in patients, but a decrease in dat angle was detected. Ulnar loop was significantly higher in the patients but they had a lower arch number. Dermatoglyphic signs were significantly different in FMF patients compared to controls.
Discussion: The nature of dermatoglyphic samples of the patients we obtained in this study may be specific for FMF. Such studies can contribute to screening and evaluating populations for the risk of disease. The relation of dermatoglyphic findings with the severity and clinical course of the disease should be a separate research topic.

Keywords
FMF; Dermatoglyphic; Fingertip lines; Ridge count; Palm angle

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Introduction

Familial Mediterranean Fever (FMF) is an autosomal recessive auto-inflammatory disease characterized by recurrent fever, peritonitis, pleuritis, arthritis and erysipelas-like rash [1]. It is the most frequent autoinflammatory disease all over the world [2]. FMF is more common among Turkish, Armenian, Arab and Sephardic Jews living around the Mediterranean region [3]. Mutations of the MEFV gene located on the short arm of chromosome 16 are responsible for the disease [4]. This gene encodes a protein called marenostrin or Pyrin [5]. Mutant pyrin is associated with inflammatory process and overproduction of Interleukin 1β [6]. An important complication of FMF is the development of AA amyloidosis which may lead to chronic kidney disease and kidney failure [7].

Dermatoglyphics is the study of fingerprint patterns and essentially, it is associated with skin patterns of the inferior surfaces of the hands and feet [8]. Dermatoglyphics is a concept formed from Greek words and "Dermato" refers to the skin, "Glyphics" means

carving [9]. As a term, it defines an analysis of a system of cutaneous ridges and grooves flowing in different directions on fingers, palmar and plantar surfaces [10]. The dermal ridge differentiation occurs in an early stage in the process of intrauterine development. These ridge patterns are associated with genetic and environmental factors [11].

FMF is a genetic disease. It is likely that specific dermatoglyphic properties may be present in FMF patients. In this context, we analyzed the dermatoglyphic signs of FMF patients with homozygous or compound heterozygous mutations and compared with the control group.

Material and Methods

This study was carried out between June 2018 and January 2019 at Cumhuriyet University, Faculty of Medicine, Department of Medical Genetics and Anatomy, Sivas, Turkey. It was approved by Cumhuriyet University Ethics Committee. Patients with dermatologic disease, and hand deformities were excluded from the study. Forty FMF patients (20 males and 20 females) who have compound heterozygous or homozygous mutation detected with the pyrosequence method and forty controls (20 males and 20 females) without any systemic disease were included in the research after giving informed consent.

Dermatoglyphic patterns were obtained using a digital scanner (CanoScan LIDE 60, Canon, Beijing, China). When taking dermatoglyphic molds, the palm was touching the scanner screen, the thumb was at approximately 30-40 degrees, and the other fingers were placed with 10-15 degrees of abduction. During scanning, 4 colored images with 300 dpi-resolution for each patient were recorded. Via images saved in jpg format, and by using the ImageJ program (NIH, Bethesda, MD, USA), fingertip sample types, fingertip ridge counts, a-b ridge count, atd, dat, and adt angles were determined. Fingertip molds were analyzed according to Cummins and Midlo classification, as whorl, ulnar loop, radial loop, and arch. The ridges were counted between the sample center and the triradius. In the samples with more than one triradius, the side that had more ridge counts was evaluated. In the samples of arch, the ridge count was accepted as zero. The ridge counts in all fingers were gathered and a total ridge count (TRC) was obtained. The axial triradius 't' emerged from the combinations of ridge bundles coming from 3 different directions between the thenar and hypothenar parts in the palm by making an angle of 120 degrees between each other.

The data obtained from the study were analyzed using SPSS version 22 (SPSS Inc., Chicago, IL, USA). The T-test, the Mann-Whitney U test, and the chi-square test were used in the statistical analysis. P values of less than 0.05 were considered as statistically significant.

Results

Forty patients with FMF and 40 healthy controls were included in the study. The female-male ratio was equal in groups. The mean age of the patients was 34.15±8.62 (range 22-58 years old) and the mean age of the controls was 24.80±6.59 (range 18-47 years old). The patients were older than the control group (p= 0.001). Based on the clinical findings and the mutation screening performed by pyrosequence, the patients were diagnosed with definite FMF.

In dermatoglyphic examination, the number of fingertip lines (except 2nd and 5th fingers on the right hand and 2nd finger on the left hand) and a-b ridge count were significantly higher in the patients than in the control group. The angle of palm atd was higher in patients, but a decrease in dat angle was detected. ($p<0.05$) (Table 1).

The ulnar loop was the most common sample in both groups, whereas the radial loop was minimal. The number of ulnar loop was significantly higher in patients with FMF than controls in both right and left hands (p= 0.001 and p= 0.045). In the right hand, the number of arch samples was significantly lower in the patients than in the control group (p= 0.008) (Table 2,3).

While the a-b ridge count in both the right and left-hand of the females with FMF showed a statistically significant increase, the increase in the number of fingertip lines was statistically significant only in the left-hand thumb. In palmar angles, the left-hand dat angle was lower than in the control group ($p<0.05$). A total number of lines and a-b ridge count was significantly increased in right and left-hands of males with FMF ($p<0.05$). On the other hand, the number of lines on the fingertip samples in male patients was higher than controls statistically except for the right-hand small finger and the left-hand middle finger. ($p<0.05$). The angle of atd from palmar angles was higher in both hands of males with FMF than healthy controls, whereas dat angle was lower. ($p<0.05$).

Discussion

Familial Mediterranean fever is one of the periodic fever syndromes caused by mutations of MEFV gene [12]. It is the most common form of hereditary inflammatory periodic disease, characterized by recurrent, self limited attacks of fever, abdominal and joint pain with serositis [13]. MEFV gene encodes Pyrin which is effective in the innate immune system and mutations of this gene cause an increase in interleukin 1 (IL-1) levels, therefore inflammation [5].

Dermatoglyphics is the term that refers to the examination of fingerprints, firstly defined by Harold Cummins in 1926 [14]. It can be said that finger, palm and sole patterns are the products

Table 1. The number of fingertip lines, palm ridge count and palmar angles in the patients with FMF and control group.

	Patient group (n=40) Right-hand Mean±SD	Control group (n=40) Right-hand Mean±SD	t	P	Patient group (n=40) Left-hand Mean±SD	Control group (n=40) Left-hand Mean±SD	t	P
Thumb	19.50±5.93	15.12±5.08	3.542	0.001*	19.82±5.14	14.92±4.29	4.626	0.000*
Index finger	15.72±7.74	12.85±6.38	1.811	0.074	14.17±7.24	11.97±6.17	1.462	0.148
Middle finger	15.70±5.61	12.07±6.45	2.680	0.009*	14.75±6.81	11.70±6.57	2.037	0.045*
Ring finger	16.62±5.34	13.57±5.86	2.431	0.017*	17.70±7.31	13.45±6.26	2.791	0.007*
Little finger	14.37±3.64	13.30±4.87	1.117	0.268	15.47±4.84	13.52±4.24	1.915	0.059*
Total ridge count	80.60±23±14	66.67±22.71	2.716	0.008*	80.85±23.19	65.55±21.36	3.069	0.003*
atd angle (o)	44.00±4.64	42.05±4.82	1.836	0.070*	45.58±5.17	40.38±4.30	4.891	0.000*
dat angle (o)	57.24±5.03	60.38±6.03	-2.531	0.013*	56.59±5.12	61.36±5.29	-4.096	0.000*
adt angle (o)	78.75±5.39	77.15±4.46	1.447	0.152	77.81±4.39	78.00±4.98	-0.178	0.859
a-b ridge count	44.80±5.57	36.15±6.84	6.195	0.000*	49.45±6.13	37.12±6.62	8.632	0.000*

Table 2. The distribution of dermal samples in the right- and left-hand fingertips of females in patients and controls.

	Samples in the right-hand fingertips of the female patients and controls								Samples in the left-hand fingertips of the female patients and controls							
	Patient group (n=20)				Control group (n=20)				Patient group (n=20)				Control group (n=20)			
	W	UL	RL	A	W	UL	RL	A	W	UL	RL	A	W	UL	RL	A
Thumb	9	10	0	1	10	9	0	1	10	10	0	0	6	14	0	0
Index finger	4	12	1	3	9	4	4	3	7	9	1	3	9	4	2	5
Middlefinger	5	14	0	1	4	11	1	4	4	12	2	2	4	9	1	6
Ring finger	7	12	1	0	10	7	1	2	3	14	1	2	4	14	0	2
Littlefinger	4	16	0	0	4	14	0	2	3	15	1	1	1	18	0	1
Total	29	64	2	3	37	45	6	12	27	60	5	8	24	39	3	14

W: Whorl, UL: Unlar loop, RL: Radial loop, A: Arch

Table 3. The distribution of dermal samples in the right- and left-hand fingertips of males in patients and controls.

	Samples in the right-hand fingertips of the male patients and controls								Samples in the left-hand fingertips of the male patients and controls							
	Patient group (n=20)				Control group (n=20)				Patient group (n=20)				Control group (n=20)			
	W	UL	RL	A	W	UL	RL	A	W	UL	RL	A	W	UL	RL	A
Thumb	11	9	0	0	14	5	0	1	13	7	0	0	16	4	0	0
Index finger	14	4	1	1	13	3	2	2	8	8	2	2	13	4	3	0
Middle finger	3	16	0	1	8	9	1	2	4	14	0	2	7	12	0	1
Ring finger	9	10	0	1	12	6	0	2	9	10	0	1	8	9	0	3
Little finger	4	16	0	0	5	15	0	0	3	16	0	1	3	17	0	0
Total	41	55	1	3	52	38	3	7	37	55	2	6	47	46	3	4

of both the environment and heredity [15]. Numerous studies which were performed in North America, Europe, East Asia and elsewhere, suggested that fingerprint patterning was a partially inherited characteristic that could be used to investigate genetic connections between populations [16]. Although there are no two people with the same dermatoglyphic signs, dermatoglyphic properties show a significant correlation within the family, and certain human groups [17]. The epidermal ridges are composed in the same period when neuronal development occurs in the intrauterine life of a fetus. Thus, dermatoglyphics is correlated with genetic conditions and may be useful in the diagnosis of a lot of medical disorders such as Klinefelter syndrome, Down syndrome, Turner syndrome, schizophrenia, diabetes mellitus type II, hypoparathyroidism [18]. The similarity of finger pattern types in monozygotic twins appears to be more pronounced than in dizygotic twins, which suggests the effect of genetic factors in the formation of fingertip patterns [19].

In a study by Chakravathy et al., the mean “atd” angle was higher and whorls were more frequent in hypertensive cases than controls. In this context, the distribution of dermatoglyphic patterns was statistically significant in patients with hypertension compared to the control group [20]. Ma et al. found significantly greater a-b ridge counts for both hands in nonsyndromic cleft lip and/or palate patients compared with the control [21]. Sabancıogulları et al. revealed that there was a statistically significant increase in the a-b ridge count,

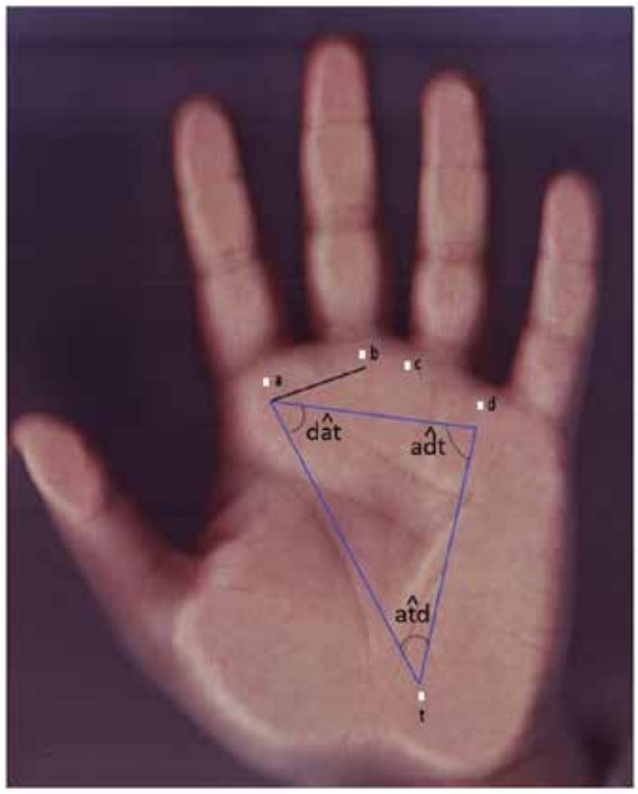

Figure 1. Image of palmar dermatoglyphic samples. The triradius in proximal of each finger was denoted by the letters a, b, c, d starting from the index finger. Axial triradius was represented by the letter t. The angles atd, adt, and dat were formed by lines between digital triradii a, d and axial triradius t, and a line from digital triradius a to digital triradius d. The a-b ridge counts were found by counting the dermal lines between triradius a and b.

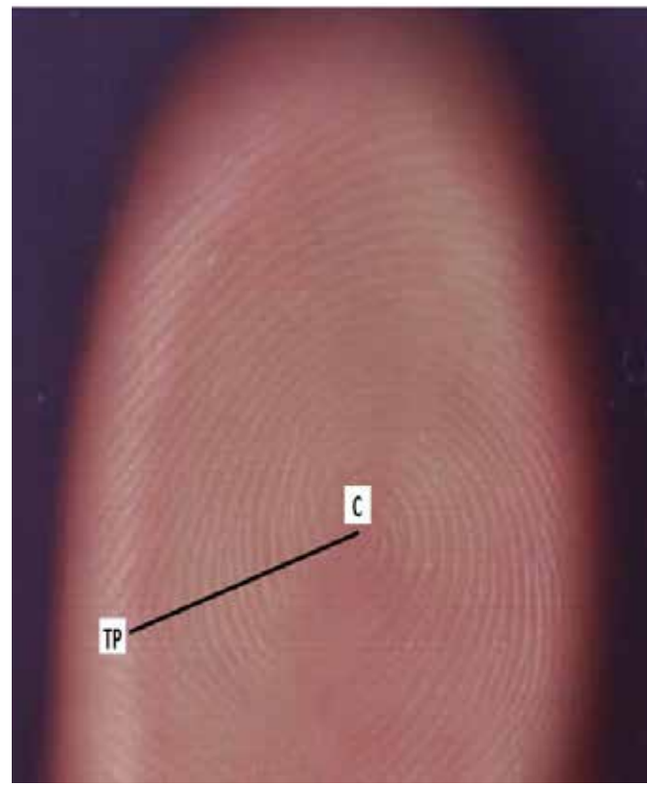

Figure 2. A fingerprint with one triradial point. A vertical line was formed to the triradius farthest from the center of the dermal sample. The number of dermal lines intersecting this vertical line was counted and the number of lines in the sample was determined.
TP: Triradial point
C: Core (Sample center)

total ridge count on both hands of patients with multiple sclerosis [22]. On the other hand, in predictive analysis of palmar dermatoglyphics in patients with breast cancer, ATD-angles showed a statistically significant difference between the patients and the control group, and the frequency of axial triradius in breast cancer patients was different from the phenotypic healthy population [23].

Yang et al. suggest that whorl-shaped fingerprints are inherited from a single gene or a group of closely linked genes. Since dermatoglyphic patterns of a human fingertip can be controlled by genetic factors, possible differences reflect the genetic diversity of individuals [8]. Dermatoglyphics have a high level of inheritance and fingertip pattern is an example of human polygenic trait [24].

FMF is a hereditary autoinflammatory disease. In this context, we investigated the dermatoglyphic findings of FMF patients and whether these findings could form a specific pattern in terms of this disease.

Genetic conditions may play an important role in the formation of ridge configurations [25]. We found that a-b ridge count and the number of fingertip lines in FMF patients were higher than in the control group. Finger ridge count is one of the most hereditary anthropometric signs, and it can be used for the study of human quantitative genetics [10]. The angle of palm atd was statistically higher but dat angle was lower in our patients. Ulnar loop was significantly higher in the patients than controls in terms of right anf left hand but patients had lower arch number in both hands and it is statistically significant in the right hand. These changes can be considered as a template for FMF patients. In a study conducted by Manikandan et al., the numbers of arch, loop and whorl showed a significant difference between blood groups [26]. In this regard, there was a considerable difference between patient and control groups in terms of ulnar loop in both hands and arch in right hand in our study. Radial loop and Whorl count did not differ between the groups.

In conclusion, deviations in dermatoglyphic samples are not diagnostic but may reflect genetic predisposition in FMF disease. The susceptibility to FMF disease can be determined by analysis of dermatoglyphic findings. The relationship between clinical findings, course of the disease and dermatoglyphic signs in FMF patients should also be investigated.

Scientific Responsibility Statement
The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest
None of the authors received any type of financial support that could be considered potential conflict of interest regarding the manuscript or its submission.

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